Appl. No. 10/076,967
Amdt. dated April 23, 2007
Amendment under 37 CFR 1.116 Expedited Procedure
Examining Group 1631

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-54 (canceled)

55 (currently amended): A method of ~~comparing the correlation between gene and protein expression~~ correlating gene expression with protein expression in two or more biological samples, the method comprising the steps of:

a) obtaining two or more biological samples;

b) generating a gene expression profile of each sample;

c) determining the nucleotide sequence of ~~an~~ at least one mRNA in each gene expression profile;

d) predicting the amino acid sequence of the polypeptide encoded by the mRNA in each gene expression profile;

e) predicting the mass of the polypeptide encoded by the mRNA in each gene expression profile;

f) generating a protein profile of polypeptides in each sample by mass spectrometry; and

g) determining the presence ~~or absence~~ in each protein profile of a polypeptide having a mass that ~~correlates to~~ is the same as the predicted mass of the encoded polypeptide, thereby identifying ~~a~~ at least one protein that is ~~or is not~~ expressed from a corresponding mRNA in each biological sample,

thereby ~~comparing the correlation between~~ correlating gene expression with ~~and~~ protein expression in two or more biological samples.

56 (previously presented): The method of claim 55, wherein one of the biological samples comprises a cell lysate from a healthy cell.

57 (previously presented): The method of claim 55, wherein one of the biological samples comprises a cell lysate from a pathological cell.

58 (previously presented): The method of claim 55, wherein one of the biological samples comprises a cell lysate from a cell contacted by a toxic compound.

59 (previously presented): The method of claim 55, wherein one of the biological samples comprises a cell lysate from a cell of a subject who responds to a drug treatment.

60 (previously presented): The method of claim 55, wherein one of the biological samples comprises a cell lysate from a cell of a subject who does not respond to a drug treatment.

61 (previously presented): The method of claim 55, wherein the biological samples comprise human cells.

62 (previously presented): The method of claim 55, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with a nucleic acid array.

63 (previously presented): The method of claim 55, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with an oligonucleotide array.

64 (previously presented): The method of claim 55, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with an mRNA array.

65 (previously presented): The method of claim 55, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with an EST array.

66 (previously presented): The method of claim 55, wherein the step of generating the gene expression profile comprises identifying expressed mRNA with a northern blot or a dot blot.

67 (canceled)

68 (previously presented): The method of claim 55, wherein two biological samples are derived from a normal cell and a pathologic cell.

69 (previously presented): The method of claim 68, wherein the pathologic cell is a cancer cell.

70 (previously presented): The method of claim 55, wherein two biological samples are derived from a healthy cell and a cell exposed to a toxic compound.

71 (previously presented): The method of claim 55, wherein mass spectrometry is laser desorption/ionization mass spectrometry.

72 (previously presented): The method of claim 55, wherein mass spectrometry is electrospray mass spectrometry.

73 (previously presented): The method of claim 55, further comprising,

in step d), after predicting the amino acid sequence of the polypeptide encoded by the mRNA in each gene expression profile, predicting a post-translational modification of the encoded polypeptide;

in step e), after predicting the mass of the polypeptide encoded by the mRNA in each gene expression profile, predicting the mass of the encoded polypeptide to reflect the post-translational modification; and

in step g), after determining the presence or absence in each protein profile of a polypeptide having a mass that correlates to the predicted mass of the encoded polypeptide,

determining the presence or absence of a polypeptide having a mass that correlates to the predicted mass of the encoded polypeptide having the post-translational modification.

74 (previously presented): The method of claim 73, wherein the post-translational modification is phosphorylation or glycosylation.

75 (currently amended): The method of claim 55 further comprising:

(i) after step [[(]]d), predicting at least one physio-chemical characteristic of the polypeptide encoded by the mRNA in each gene expression profile selected from the group consisting of isoelectric point, hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope sequence, ligand binding sequence, and metal chelate binding;

(ii) fractionating the polypeptides in each sample according to the at least one physiochemical characteristic, retaining the fraction containing the predicted physiochemical property, and then generating a protein profile of polypeptides in each sample by mass spectrometry in step [[(]]f); and

(iii) in step [[(]]g), correlating the predicted mass and the at least one physiochemical characteristic of each polypeptide encoded by the mRNA in each gene expression profile with a polypeptide in each respective protein expression profile.

76 (previously presented): The method of claim 75, wherein the physio-chemical characteristic is isoelectric point and fractionating the polypeptides comprises isoelectric focusing.

77 (previously presented): The method of claim 75, wherein the physiochemical characteristic is isoelectric point and fractionating the polypeptides comprises capturing polypeptides on a solid phase-bound ion exchange adsorbent, washing away unbound polypeptides and detecting the bound polypeptides by laser desoprtion/ionization mass spectrometry.

78 (previously presented): The method of claim 75, wherein the physiochemical characteristic is hydrophobicity and fractionating the polypeptides comprises capturing

polypeptides on a solid phase-bound hydrophobic interaction adsorbent, washing away unbound polypeptides and detecting the bound polypeptides by laser desoprtion/ionization mass spectrometry.

79 (previously presented): The method of claim 75, wherein the physiochemical characteristic is hydrophilicity and fractionating the polypeptides comprises capturing polypeptides on a solid phase-bound hydrophilic interaction adsorbent, washing away unbound polypeptides and detecting the bound polypeptides by laser desoprtion/ionization mass spectrometry.

80 (previously presented): The method of claim 75, wherein the physiochemical characteristic is epitope sequence and fractionating the polypeptides comprises capturing polypeptides on a solid phase-bound biospecific adsorbent, washing away unbound polypeptides and detecting the bound polypeptides by laser desoprtion/ionization mass spectrometry.

81 (previously presented): The method of claim 75, wherein the physiochemical characteristic is metal chelate binding and fractionating the polypeptides comprises capturing polypeptides on a solid phase-bound immobilized metal chelate adsorbent, washing away unbound polypeptides and detecting the bound polypeptides by laser desoprtion/ionization mass spectrometry.